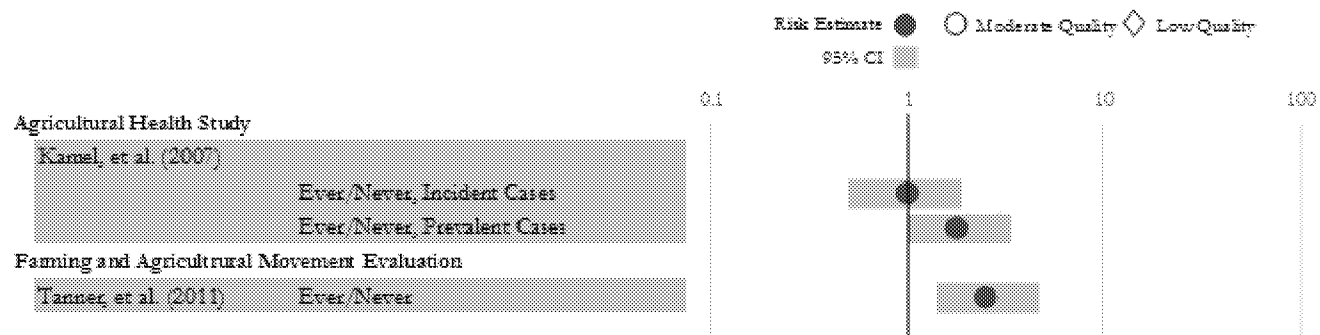


Message

**From:** Niman, Aaron [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=A8893877540D416D880562DD19AB78A4-NIMAN, AARO]  
**Sent:** 1/18/2018 7:28:56 PM  
**To:** Susan Viet [SusanViet@westat.com]  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

This looks good – nice work!

One minor comment – there is an extra row for the Kamel et al (2007). See below.



**From:** Susan Viet [mailto:SusanViet@westat.com]  
**Sent:** Thursday, January 18, 2018 2:10 PM  
**To:** Niman, Aaron <niman.aaron@epa.gov>  
**Subject:** Fw: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Aaron: Please see the next version. We have re-assigned van der Mark to Moderate Quality so we have no High Quality PD studies. Let us know if this works for tomorrow's deliverable. Susan

**From:** Rebecca Birch  
**Sent:** Thursday, January 18, 2018 1:39 PM  
**To:** Susan Viet  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Hi Susan,

How's this? I removed the multiple colors since we no longer have a high quality study. I used diamonds for low quality. I am thinking of removing some of the blank rows, while they make nice breaks between studies/papers, they make it too long for the regular size paper.

I don't think Brouwer is a reanalysis since the exposure is different from van der Mark. I also checked the 2 Firestone articles and the second had 4 more year, thus I didn't note that one as secondary. This aligns with what Aaron has in his table.

Rebecca

**From:** Susan Viet  
**Sent:** Thursday, January 18, 2018 1:10 PM  
**To:** Niman, Aaron <niman.aaron@epa.gov>

**Cc:** Rebecca Birch <RebeccaBirch@westat.com>  
**Subject:** Re: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Oh, now I understand. I think we can delete that footnote. Thanks.

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**From:** Niman, Aaron <niman.aaron@epa.gov>  
**Sent:** Thursday, January 18, 2018 1:07 PM  
**To:** Susan Viet  
**Cc:** Rebecca Birch  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

The footnote relates to my previous comments (about grouping studies) in this email chain and was intended to identify results that are based on study data that has previously been reported and not completely independent.

I generally relied on your large summary table, but please feel free to select the effect estimates that you think are most appropriate.

-Aaron

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**From:** Susan Viet [mailto:SusanViet@westat.com]  
**Sent:** Thursday, January 18, 2018 10:31 AM  
**To:** Niman, Aaron <niman.aaron@epa.gov>  
**Cc:** Rebecca Birch <RebeccaBirch@westat.com>  
**Subject:** Re: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

I think it's clear - you'd like the lighter shade to be in the left hand columns as well as the right hand columns. We'll send a copy when we have revised.

Also, your footnote refers to estimates from a secondary analysis - not sure then if values vary from our articles, but can you please send the reference and we'll add it in.

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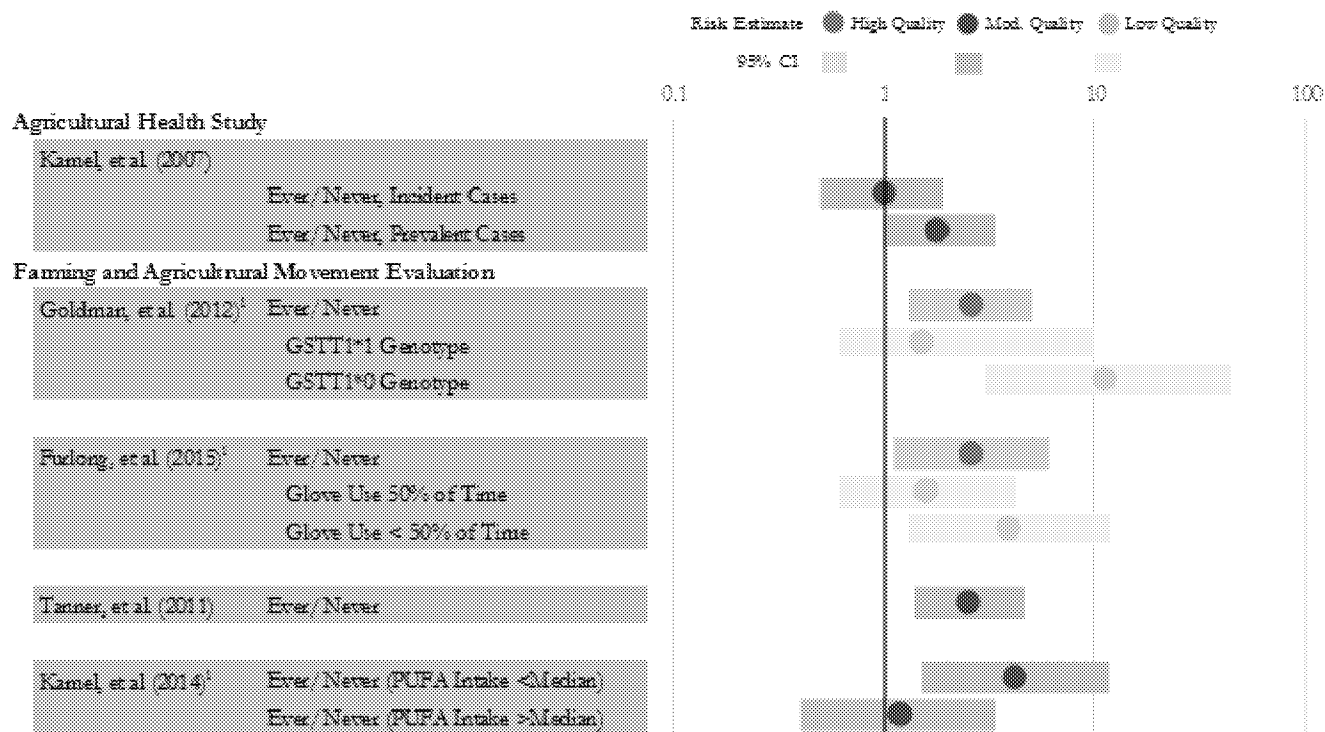
**From:** Niman, Aaron <niman.aaron@epa.gov>  
**Sent:** Thursday, January 18, 2018 10:24 AM  
**To:** Susan Viet  
**Cc:** Rebecca Birch  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

I am not sure I am being clear.

For AHS/FAME, all Ever/Never comparisons are currently in a bolder color (see red arrows below). I am suggesting to keep Tanner et al in the bolder color, but fade all the other comparisons because they are essentially secondary analysis or further stratification of the results reported by Tanner (correct me if this is wrong). While Kamel is related, I think it is OK to also keep bolded as you have already.

More generally, what I am suggesting is to make the primary effect estimates for each study group more prominent . These are typically Ever/Never comparisons, but I recognize there are some exceptions.

Let me know if you think this is confusing or can't be done consistently.



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**From:** Susan Viet [<mailto:SusanViet@westat.com>]  
**Sent:** Thursday, January 18, 2018 10:03 AM  
**To:** Niman, Aaron <[niman.aaron@epa.gov](mailto:niman.aaron@epa.gov)>  
**Cc:** Rebecca Birch <[RebeccaBirch@westat.com](mailto:RebeccaBirch@westat.com)>  
**Subject:** Re: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Clarification - We had FAME studies in the lighter shade since these are part of AHS , but we can treat as a separate study.

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**From:** Susan Viet  
**Sent:** Thursday, January 18, 2018 9:59 AM  
**To:** Niman, Aaron  
**Cc:** Rebecca Birch  
**Subject:** Re: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Thanks Aaron, We'll work from these comments. Susan and Rebecca

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**From:** Niman, Aaron <[niman.aaron@epa.gov](mailto:niman.aaron@epa.gov)>  
**Sent:** Thursday, January 18, 2018 9:42 AM  
**To:** Susan Viet  
**Cc:** Rebecca Birch  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Hi Susan,

Sorry for the delay. Per my Tuesday email, let's stick with the second figure and detailed tabular information as an appendix.

Here are some other revisions to the figure:

- Within study groups (e.g., FAME), please order studies by study year. Conveniently for AHS, FAME and PEG, the first publication by each group included the main Never/Ever Exposure comparison that is of most interest to EPA.
- I like how you have faded the color scheme for secondary analysis. I suggest completely fading all studies that were secondary analysis. For FAME studies, for example, Tanner et. al 2011 would be a bolder color than the other studies. Let me know if you think this makes sense.

Thanks,

-Aaron

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**From:** Susan Viet [<mailto:SusanViet@westat.com>]  
**Sent:** Wednesday, January 17, 2018 5:34 AM  
**To:** Niman, Aaron <[niman.aaron@epa.gov](mailto:niman.aaron@epa.gov)>  
**Cc:** Rebecca Birch <[RebeccaBirch@westat.com](mailto:RebeccaBirch@westat.com)>  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Thanks Aaron, We'll look forward to hearing from you. No problem on including the details in a table in the Appendix.  
Susan

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**From:** Niman, Aaron [<mailto:niman.aaron@epa.gov>]  
**Sent:** Tuesday, January 16, 2018 9:55 PM  
**To:** Susan Viet <[SusanViet@westat.com](mailto:SusanViet@westat.com)>  
**Cc:** Rebecca Birch <[RebeccaBirch@westat.com](mailto:RebeccaBirch@westat.com)>  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Hi Susan,

I generally agree that the simpler the better, and visually prefer the first graph, but I think it is important to emphasize that not all the study cohorts/results are independent. I will touch base with others at EPA and provide some additional feedback COB Wednesday.

Also, I think the more detailed tabular information will be helpful for us to have access if we want to further evaluate. Given that the data is already in tabular format, can you add a more detailed table as to the appendix (with numerical values, No. Cases/Controls, and Study Quality) and cross-reference with the forest plot that will be added to the main body of the text?

Thanks,

-Aaron

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**From:** Susan Viet [<mailto:SusanViet@westat.com>]  
**Sent:** Tuesday, January 16, 2018 1:56 PM  
**To:** Niman, Aaron <[niman.aaron@epa.gov](mailto:niman.aaron@epa.gov)>  
**Cc:** Rebecca Birch <[RebeccaBirch@westat.com](mailto:RebeccaBirch@westat.com)>  
**Subject:** Re: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Hi Aaron:

Rebecca Birch (who I think you know from the weekly reporting) has worked a bit on a visual for the PD estimates. We both like your Forest plot but thought there might be a way to simplify and include study quality.

Please find attached 2 versions for your input. We liked the first one due to its simplicity, but feel it 'over weights' studies with multiple rows, so tried version 2.

Rebecca feels the simpler the graphic the better. The more the eye has to move around and find things, the harder the graphic is for people. The more information on a graphic, the more likely a table would be preferable. Thus she prefers the first one, maybe with some edits to match the left half (words) with the left half of the new one. She likes it ordered by quality and colors used to highlight significance, assuming those are the things readers care about.

As neither includes all the information in your figure, two other suggestions are:

- We use one of Rebecca's figures, and include your table with the numerical information (Cases/Controls, Estimate, LCL, UCL information).
- We color code (and use different shapes for) the point estimates in your figure, e.g., a circle for High, triangle for Moderate, and square for Low. Then there is only one figure for the reader to look at, packed with a lot of information.

We look forward to your thoughts,

Susan and Rebecca

PS: Please pay no attention to the quality assignments, Rebecca was using the old scoring, as well as the data in your figure, which is missing the van der Mark article, and it looks like a few more notes may need updating.

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**From:** Niman, Aaron [<mailto:niman.aaron@epa.gov>]  
**Sent:** Friday, January 12, 2018 11:00 AM  
**To:** Susan Viet <[SusanViet@westat.com](mailto:SusanViet@westat.com)>  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Thanks Susan – I know you will be delivering the final report next Friday. Don't hesitate to contact me if there any loose-ends that could use immediate feedback from EPA to address.

-Aaron

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**From:** Susan Viet [<mailto:SusanViet@westat.com>]  
**Sent:** Friday, January 12, 2018 10:57 AM  
**To:** Niman, Aaron <[niman.aaron@epa.gov](mailto:niman.aaron@epa.gov)>  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

I concur, we'll make it clear...

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**From:** Niman, Aaron [<mailto:niman.aaron@epa.gov>]  
**Sent:** Friday, January 12, 2018 10:52 AM  
**To:** Susan Viet <[SusanViet@westat.com](mailto:SusanViet@westat.com)>  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Let's keep them in the table, but make it clear that no paraquat-specific results are reported. If it is hard to make this clear, then they can just be removed.

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**From:** Susan Viet [<mailto:SusanViet@westat.com>]  
**Sent:** Friday, January 12, 2018 10:48 AM  
**To:** Niman, Aaron <[niman.aaron@epa.gov](mailto:niman.aaron@epa.gov)>  
**Subject:** Re: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Would you like these 3 to remain in the big table as well then? Susan

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**From:** Niman, Aaron <[niman.aaron@epa.gov](mailto:niman.aaron@epa.gov)>  
**Sent:** Wednesday, January 10, 2018 1:33 PM  
**To:** Susan Viet; Karen Della Torre  
**Cc:** Hudgens, Edward; Aldridge, Ashlee; Miller, David  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Thanks Susan,

Re: Gorell 1998, Rajput 1987, and Rugberg 2011 -- I think we can keep the individual reviews in the appendix of the report and make a footnote in the main body of the report that the papers were reviewed, but did not include paraquat-specific analysis.

Also oddly, I will note that Rugberg (2011) was included in a meta-analysis (<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0151841>) that looked at a number of environmental factors (cigarette smoking, rural living, well water consumption, farming, pesticide use, and paraquat exposure). I tried finding the effect estimate reported for Rugberg (2011) in this paper and could not find it. Specifically, the authors report a RR of 1.01 (0.2 – 5.01) for Rugberg for ever use of paraquat.

-Aaron

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**From:** Susan Viet [<mailto:SusanViet@westat.com>]  
**Sent:** Wednesday, January 10, 2018 11:36 AM  
**To:** Niman, Aaron <[niman.aaron@epa.gov](mailto:niman.aaron@epa.gov)>; Karen Della Torre <[DELLATK1@WESTAT.COM](mailto:DELLATK1@WESTAT.COM)>  
**Cc:** Hudgens, Edward <[Hudgens.Edward@epa.gov](mailto:Hudgens.Edward@epa.gov)>; Aldridge, Ashlee <[Aldridge.Ashlee@epa.gov](mailto:Aldridge.Ashlee@epa.gov)>; Miller, David <[Miller.DavidJ@epa.gov](mailto:Miller.DavidJ@epa.gov)>  
**Subject:** Re: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Aaron: Just a follow-up on the Paraquat table,

-Per your recommendations, we will remove Gorell 1998, Rajput 1987, and Rugberg 2011 from the review (we had assigned Gorrell and Rugberg *Don't Know* during screening with a note that it appeared only general pesticide use was analyzed; oddly Rajput specifically calls out paraquat in the abstract even though they do not analyze it separately in the article). This brings us down to 44 articles to be included in the Synthesis report.

- The review team agrees with your comments on study quality and these have been changed (the one exception is Waggoner, we have left D as 2, a prospective design is good, but lowered E and B for reasons stated). We will use these final assignments in the Synthesis report.

Please let us know if you have any concerns with these items.

Thanks,  
Susan

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**From:** Niman, Aaron <niman.aaron@epa.gov>  
**Sent:** Friday, December 22, 2017 3:18 PM  
**To:** Susan Viet; Karen Della Torre  
**Cc:** Hudgens, Edward; Aldridge, Ashlee; Miller, David  
**Subject:** RE: WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Susan and Karen,

Attached please find our review comments and input on the draft synthesis report submitted for our review on Dec 2. They are provided in the following attachments:

| Attachment   | Notes   |
|--|---|
| 1. Paraquat_Synthesis Report_11282017_DRAFT_EPA Comments_Send.docx | Provides detailed comments in Tracked Changes and includes text for EPA placeholder sections  |
| 2. Paraquat table 12172017 (All)_EPA Comments_Send.xlsx            | Provides comments on scoring in column AC. In general, these comments focus on making scoring consistent across studies, but sometimes include more detailed comments on specific studies.  |
| 3. PD Forest Plot Template_EPA_Send.xlsx                           | Provides forest plot example we think would be helpful to include in the Parkinson's section of the report. I have attempted to extract the correct effect estimate and proposed a way to group studies. You and your staff may have a better sense of the appropriate effect estimate, so please update this table as appropriate. |

In addition, here are additional comments that we thought would be helpful to provide in this email:

#### Overall Impressions

- The report is consistent with the format you proposed. It is well organized and easy to follow the approach used to perform the literature review.
- The Parkinson's Disease section includes a lot of different studies and results – it's a lot for the reader to process, so we would like to see a summary plot to summarize the results and make it more obvious if there is an imbalance in reported results. I have attempted to do this in the attached Forest Plot, but am open to suggestions on your end.
- The Summary section is somewhat general in terms of gaps/limitations. This could be strengthened by organizing by some key themes, which I have I tried to highlight in our Tracked Changes comments. The Summary section could also be strengthened by better relating to the evaluation described in Section 3 (and the individual reviews). For example, it would be helpful to cross-reference studies as examples when describing strengths/limitations/gaps.

#### Comments on Scoring Approach

- I have made a comment suggesting to change the scoring scheme to: Low (0-4), Moderate (5-8), High (9-12). My thinking is that it's unlikely that a published study would have a score of 0, so this would make the scoring distribution across more equal across categories. Let me know your thoughts and if you have reservations about making this change.
- In some cases, we though the scoring was done inconsistently. We have tried to call attention to this in the large summary table (Attachment 2), but here are some specifics:
  - GIS approaches were score 0 or 1. We think a score of 0 is consistent with the study quality table because the measure is not individual-level/nor validated.

- Cross-Sectional study design were scored 0 or 1. We think a score of 0 is consistent with the study quality table.

### Comments on Study Reviews

- In general, it looks like the study reviews have been updated to reflect our previous comments (i.e., restructure Evaluation section, add sample size/count information, better paraphrase source material).
- Specific Comments on Study Reviews:
  - A few epi summaries (Monge et al. 2007) reported statistically significant results for ORs, RRs, etc. when the 95% confidence interval included the null value of 1.0. We consider 95% CIs that do not include the null value of 1.0 (i.e. any number > 1.0) to be statistically significant.
  - Hertzman et al. 1990 – study could not calculate ORs for paraquat exposure (since 0 controls were reported), however the study quality was ranked as ‘moderate’.
  - Kamel et al. 2014 – number of cases and controls were not provided in the description of “**Effect Measure and Point Estimates**”
  - Schenker et al. 2004 – number of cases and controls were not provided in the description of “**Effect Measure and Point Estimates**”
  - Lee et al. (2012) – Narrative does not list number of cases/controls for TBI + Paraquat OR (AOR 3.01, 95% CI 1.51–6.01). This should be 21 and 19, respectively.
  - Waggoner et al. 2011 – This AHS study (pesticides and injury mortality) appears to be given a High score, but has fundamental problems that are noted in the review and not well reflected in the score. I have additional concerns that I will summarize here:
    - **Design:** I question if AHS’ prospective design is a strength for examining the relationship between chronic pesticide exposure (based on self-report) and an acute event like fatal injury. It seems there is a strong disconnect between the two measures because the likely risk interval for fatal injury is acute (minutes, hours, days).
    - **Exposure:** Per comment above, I question the relevance of the exposure metric in evaluating fatal injury. I question whether it is truly validated for an acute outcome like injury and, in this case, do not think that the AHS questionnaire represents a “high quality questionnaire on chemical-specific exposure assessment during relevant exposure window” (i.e., terminology used in the study quality assessment criteria).
    - **Outcome:** While NDI is a validated registry, there was no attempt to screen out injury fatalities that had causes that were unrelated to their use of pesticides (I am not familiar enough with NDI to know if this is possible). In this case, I think the outcome approach is actually fairly non-specific and any results, particularly given the multiple comparisons performed and fact that this research hypothesis is not a primary reason AHS was originally launched. Alternatively, if they had hypothesized that chronic pesticide exposure could cause a specific type of injury, and examined fatal injuries through NDI, I would have more confidence in their outcome ascertainment approach.
    - **Confounders:** Your review states, “researchers were unable to obtain any information related to the actual events/nature of the injury.” “Researchers were also unable to obtain information on risk taking behavior, so it’s not clear to me that they obtained information on confounders that could be relevant to their outcome of interest.” Seems like important confounder for outcome were not included.
    - **Bias:** Given all comments above, there seems high potential for bias.

In terms of next steps, I will be available next week after the Christmas Holiday if you want to speak immediately about our review comments.

Thanks for all your work on the paraquat review.

Regards,

-Aaron



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**From:** Susan Viet [<mailto:SusanViet@westat.com>]

**Sent:** Saturday, December 2, 2017 1:22 PM

**To:** Niman, Aaron <[niman.aaron@epa.gov](mailto:niman.aaron@epa.gov)>; Aldridge, Ashlee <[Aldridge.Ashlee@epa.gov](mailto:Aldridge.Ashlee@epa.gov)>; Miller, David <[Miller.DavidJ@epa.gov](mailto:Miller.DavidJ@epa.gov)>

**Cc:** Hudgens, Edward <[Hudgens.Edward@epa.gov](mailto:Hudgens.Edward@epa.gov)>; Karen Della Torre <[DELLATK1@WESTAT.com](mailto:DELLATK1@WESTAT.com)>; Susan Viet <[SusanViet@westat.com](mailto:SusanViet@westat.com)>

**Subject:** WA 4-02 (Air), Task 4, Deliverable 8 (Draft)

Hi all,

Attached is the draft synthesis report for WA 4-02 (Air) Task 4, Deliverable 8, draft.

We look forward to working with EPA in finalizing the individual study summaries, table of key study information, and this synthesis report.

Please let us know if you have any questions,

Susan

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Susan Marie Viet, PhD, CIH, CET  
Senior Environmental Health Scientist  
Westat  
Phone: (301) 610-5514  
Email: [SusanViet@westat.com](mailto:SusanViet@westat.com)